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**AUSTRALIA**
**Patents Act 1990**

# PROVISIONAL SPECIFICATION

Invention Title: DETECTING SUBTLE COGNITIVE IMPAIRMENT

Applicant: MONASH UNIVERSITY

The invention is described in the following statement:

# Detecting Subtle Cognitive Impairment

## Field of Invention

The invention relates to a method of assessing cognitive impairment. More particularly, it relates to a method of assessing cognitive impairment that involves the presentation of a visual stimulus to a user and subsequent assessment of the user's response.

## Background to the Invention

There are a number of neuropsychological tests that have been developed to diagnose and measure cognitive impairment. Typically, methods of assessing subjects for cognitive impairment have allowed subjects to respond at their own leisure. This was done primarily because the primary aim is to estimate cognitive processing speed independently of motor ability. The monitoring of the time taken for the user to respond was therefore seen as introducing an error factor into any estimation of cognitive impairment.

A major disadvantage of this type of test for detecting cognitive impairment was that it tended to suffer from a lack of sensitivity making it unsuitable for the detection of mild cognitive impairment and small variations in cognitive ability over time.

The methods of the prior art tended to be time-consuming methods that involved gradually changing the duration over which a stimulus was presented until a predetermined error rate was achieved. The methods of the prior art had a relatively limited statistical power because they produce only a single score for each test subject instead of a response curve. The methods of the prior art generally used masks that were ineffective at completely blocking out an afterimage of a previously presented stimulus. The methods of the prior art did not include a test of visual impairment to control for the possibility that impaired vision might have influenced the performance of test subjects. The methods of the prior art also tended to result in a learning effect such that the testing

methods could not be repeated on the test subject without a considerable interval between tests. Such methods also tended to require specially trained personnel to assess the results and make a subjective evaluation of the subject. This is disadvantageous in that the introduction of a subjective element provides the potential for error, which is further magnified where different psychologists are involved. Where tests are conducted on a subject having characteristics differing from the norm, then there is a further problem encountered where cultural, age or gender bias influence the results.

The discussion of the background to the invention herein is included to explain the context of the invention. This is not taken as an admission that any of the material referred to was published, known as part of the common general knowledge as at the priority date of the claims.

The object of the present invention is to overcome, alleviate or minimise one or more of the problems present in the prior art methods of measuring cognitive impairment.

**Summary of the Invention**

In a first aspect of the present invention, there is provided a method of assessing cognitive impairment of a user, including the steps of:

(a) presenting a visual test stimulus to the user for a pre-determined exposure time;

(b) masking the test stimulus;

(c) measuring a response from the user, the response providing information about the user's perception of specific characteristics of the test stimulus together with the time taken for the user to respond;

(d) repeating steps (a) to (c) to develop a user profile; and

(e) comparing the user profile to a standard profile to assess cognitive impairment in the user.

Preferably, the masking of the test stimulus occurs by placing a mask over or in place of the stimulus.

The user profile may optionally be a response curve.

Step (d) may include repeating steps (a) to (c) over a range of pre-determined exposure times. Preferably, the pre-determined exposure times are the same for each of the users assessed. This will allow for a relative comparison between each of the users assessed.

In one form of the invention, the invention further includes the step of calculating a representative error rate representing the proportion of inaccurate responses for each of the pre-determined exposure times. This representative error rate can then be included in the user profile and used to assess the degree of cognitive impairment.

The user profile preferably includes an error rate curve charting the representative error rate relative to the pre-determined exposure time. This allows charting of the user's profile against the profile of cognitively normal individuals. A deviation of the user's curve from the standard corresponds to cognitive impairment.

The representative error rate may, for example, be calculated from a mean of the error of each response at the pre-determined exposure time.

Additionally or alternatively, the invention includes the step of calculating a representative response time for each of the pre-determined exposure times. Where the representative response time is calculated, the user profile may optionally include a response time curve charting the mean response relative to the pre-determined exposure time.

In a particularly preferred form of the invention, the pre-determined exposure times are equally spaced. It is also preferred that the exposure times are the same for all subjects which are tested.

The standard profile may be generated in any suitable manner. It is particularly preferred that the standard profile be generated from data obtained from or testing performed on a population of cognitively normal individuals.

The test stimulus may be presented to the user for an exposure time of between 10ms and 300 ms.

The user may preferably be given a choice between two different responses to each test stimulus, in this situation, one of the different test stimuli are presented to the user in step (a). Preferably, each of the stimuli are presented an equal number of times.

Any suitable mask may be used with the present invention. A particularly advantageous mask to use is an image including at least one full circle, preferably the image has a plurality of full circles or parts thereof.

In a second aspect of the invention, there is provided a method of assessing visual impairment of a user, including the steps of:

(i) presenting a visual test stimulus to the user for a pre-determined exposure time;

(ii) masking the test stimulus;

(iii) measuring a response from the user, the response providing information about the user's perception of specific characteristics of the test stimulus together with the time taken for the user to respond;

(iv) repeating steps (i) to (iii) at the same pre-determined exposure time to develop a user profile; and

(v) comparing the user profile to a standard profile to assess visual impairment in the user.

In a third aspect of the present invention, there is provided a method of assessing cognitive impairment of a user, including the steps of:

(i) presenting a visual test stimulus to the user for a pre-determined exposure time;

(ii) masking the test stimulus;

(iii) measuring a response from the user, the response including:

(a) a response time; and

(b) a correct or incorrect indication of the visual test stimulus;

(iv) repeating steps (i) to (iii) to develop a user profile; and

(v) comparing the user profile to a standard profile to assess cognitive impairment in the user.

In a fourth aspect of the present invention, there is provided a system for assessing cognitive impairment of a user, including:

(a) means for presenting a visual test stimulus;

(b) mask for placement over or in place of the test stimulus after presentation of the visual stimulus;

(c) response measuring means to measure the response from the user after presentation of the visual test stimulus;

(d) processing means to process the response from the user to develop the user profile; and

(e) assessment means to compare the user profile to a standard profile to assess cognitive impairment in the user.

In a fifth aspect of the present invention, there is provided a mask for masking visual test stimulus, the mask including an image having a plurality of filled circles or parts thereof.

**Brief Description of Drawings**

The invention will now be described in further detail by reference to the enclosed drawings illustrating example forms of the invention. It is to be understood that the particularity of the drawings does not supercede the generality of the preceding description of the invention. In the drawings:

Figures 1A, 1B and 1C are various screen illustrations presented to a user in one embodiment of the present invention. Figures 2A–C, 3A–C and 4A–C illustrate different forms of this embodiment of the invention.

Figures 5A, 5B and 5C are various screen illustrations presented to a user in another embodiment of the present invention. Figures 6A, 6B and 6C illustrate different forms of this embodiment of the invention.

Figure 7 is a graph showing mean error rate plotted against exposure time according to the present invention.

Figure 8 is a graph showing mean response time plotting against exposure time according to the present invention.

**Detailed Description**

One embodiment of the present invention involves presentation of two parallel lines of different length to a user or test subject. These lines are presented for a relatively short period, they are then followed by a mask consisting of filled circles. The test stimulus and subsequent mask is then repeatedly presented to the viewer at pre-determined exposure times, these exposure times are typically chosen to be between 10 ms and 300 ms. The test subject may then respond to the stimulus by pressing a button to indicate whether the short line is on the left or right hand side. A computer can then be used to record the number of responses for each exposure time together with the length of time taken for the subject to respond to the stimulus. This length of time is termed the "response time". The data obtained for each exposure time is then pooled to obtain a mean error rate and a mean response time. These mean values for each exposure time are then compared against a standard curve generated from a population of cognitively normal individuals. The inventors have found that significantly slower response times or significantly higher error rates for one or more of the exposure times tend to be indicative of a cognitive impairment. The extent of any deviation away from the standard curve can therefore be used to predict the extent of cognitive impairment.

Figure 1 illustrates the present invention showing example frames of a 200x200 pixel graphics presented in the centre of a 15 inch flat screen monitor at a resolution of 600x480. Figure 1A is an illustration of the focal point stimulus,

this is shown to the user before commencing the task. The test stimulus (as shown in Figure 1B) is then presented to the user. Each of these test stimuli can be individually presented for various durations, such as: 13, 26, 39, 52, 65, 91, 117, 143, 169, 195 or 221 ms. After presentation of the test stimulus, the stimulus is then masked with a mask as shown in Figure 1C. It is then necessary for the user to nominate whether the stimulus present has a shorter edge on the left or the right of the screen. The user's response is then recorded and compared to the actual stimulus presented. The time taken for the user to respond (as measured between presentation of the stimulus and entry of a response) is also measured. A profile of the user can then be developed by compiling information as to the user's response to the stimulus and time taken to respond.

Figures 2, 3 and 4 each illustrate the present invention with alternative test stimuli.

Figure 5 is a further illustration of a sequence presented to the user. The focal point stimulus shown in Figure 5A is presented at a duration of greater than 450 ms. One of the test stimuli shown in Figure 5B is then presented for a predetermined duration of between 10-300 ms followed by the mask shown in Figure 5C which is presented for at least 450 ms. The user is presented with instructions and informed that their task is to decide whether a small black line appears on the screen, it may appear on the left or the right of the central cross. The user then responds by pressing a button to indicate whether they detected the test stimulus to be on the right or left hand side of the screen. The results of the user's perception are then used to create a user profile which can then be matched against a standard profile to determine the degree of visual impairment. Figure 6 depicts an alternative to the presentation sequence illustrated in Figure 5 with horizontal test stimuli.

Figure 7 is a graph that plots the mean error rate (%) against exposure time using stimuli such as those illustrated in Figure 1. A Mini Mental State Exam (MMSE) score of 30 is judged to be normal while lower MMSE scores of 29-25 show subtle cognitive impairment. Figure 8 shows another graph which charts

the mean response time against the exposure time. Again, a MMSE of 30 is shown as a normal indicator while deviations from the normal of MMSE's corresponding to 29, 28 and 27 show subtle cognitive impairment.

The present invention is advantageous in that it provides a method of detecting cognitive impairment that can be applied to individuals who are considered high functioning individuals with an almost normal score of between 27-29 on a MMSE. This results from the ability to detect differences in individuals who differ by only small increments on the MMSE.

The method of the present invention is also advantageous in that it may be performed relatively quickly at a time of around 5-10 minutes. The method also requires no supervision from highly trained personnel, as there is no need for the method to be performed by a trained psychologist.

The inventors have also found that the method measures the subconscious cognitive processes in a way that is relatively free from the influence of a learning effect. Because of this, and the fact that the invention can be performed quickly, the subjects can be re-evaluated by the method several times in a day if necessary.

A further advantage of the present invention is that the method generates quantitative data that does not involve subjective interpretation. The results of the method can therefore be compared to results gathered by others where comparison of results is necessary. The method also has the advantage that it can assess a subject without age or gender bias.

The present invention can be implemented in any suitable manner. In one envisaged form the invention would be implemented through the use of a computer program operating on a standard platform such as Microsoft Windows™.

This invention has potential application in a wide variety of circumstances and is particularly applicable to detection of mild cognitive impairment or in the re-

evaluation of test subjects for changes in the degree of cognitive impairment. A person skilled in the art will realise that some possible, but not necessarily exclusive applications, of the present invention include:

(a) Measurement of cognitive performance before and after major surgical procedures, such as cardiac surgery, to detect subtle neurological complications that often arise from such procedures;

(b) Quantification of the degree and rate of recovery from instances of trauma such as head trauma from sporting or vehicle related injuries;

(c) Monitoring of the cognitive side-effects of drugs used to treat a variety of illnesses;

(d) Quantitative measurement and comparison of the effectiveness of different pharmaceutical regimes in the treatment of neurological conditions;

(e) Monitoring of mild cognitive impairment, as a precautionary screening process, in ostensibly high functioning individuals in whom mild cognitive impairment may have serious consequences. For example, an airline or fighter pilot.

(f) Detection and monitoring of cognitive decline that may be associated with the onset of a progressive neurological condition such as Alzheimer's disease.

It is to be understood that various additions, alterations and/or modifications may be made to the parts previously described without departing from the ambit of the invention.

DATED: 7 January 2003
PHILLIPS ORMONDE & FITZPATRICK
Attorneys for:
MONASH UNIVERSITY

**The claims defining the invention are as follows:**

1. A method of assessing cognitive impairment of a user, including the steps of:

(a) presenting a visual test stimulus to the user for a pre-determined exposure time;

(b) masking the test stimuli;

(c) measuring a response from the user, the response providing information about the user's perception of a characteristic of the test stimulus together with the time taken for the user to respond;

(d) repeating steps (a) to (c) to develop a user profile;

(e) assessing cognitive impairment based on the profile.

2. A method according to claim 1, wherein step (d) includes repeating steps (a) to (c) over a range of pre-determined exposure times.

3. A method according to claim 1 or 2, further including the step of calculating a representative error rate representing the proportion of inaccurate responses for each of the pre-determined exposure times.

4. A method according to claim 3, wherein the user profile includes an error rate curve charting the representative error rate relative to the pre-determined exposure time.

5. A method according to any one of claims 3 or 4 wherein, the representative error rate is calculated from a mean of the error of each response at the pre-determined exposure time.

6. A method according to any one of the preceding claims, further including the step of calculating a representative response time for each of the pre-determined exposure times.

7. A method according to claim 6, wherein the user profile includes a response rate curve charting the mean response relative to the pre-determined exposure time.

8. A method according to any one of claims 2 to 7 wherein each of the pre-determined exposure times are equally spaced.

9. A method according to any one of the preceding claims, wherein the standard profile is generated from data obtained from a population of cognitively normal individuals.

10. A method according to any one of the preceding claims, wherein the exposure time is between 10ms and 300 ms.

11. A method according to any one of the preceding claims, wherein the user has a choice between two different responses to each test stimulus.

12. A method according to claim 11, wherein one of two or more different test stimuli are presented to the user in step (a).

13. A method according to claim 12, wherein each of the stimuli are presented an equal number of times.

14. A method according to any one of the preceding claims, wherein the test stimulus is masked by a mask that includes at least one full circle.

15. A method according to claim 14, wherein the mask is an image including a plurality of full circles or parts thereof.

16. A method according to any one of the preceding claims, wherein the step of comparing the user profile to a standard profile to assess cognitive impairment in the user.

16. A method of assessing visual impairment of a user, including the steps of:

(a) presenting a visual test stimulus to the user for a pre-determined exposure time;

(b) masking the test stimulus by placing a mask over or in place of the test stimulus;

(c) measuring a response from the user, the response providing information about the user's perception of specific characteristics of the test stimulus together with the time taken for the user to respond;

(d) repeating steps (a) to (c) at the same pre-determined exposure time to develop a user profile; and

(e) comparing the user profile to a standard profile to assess visual impairment in the user.

17. A method of assessing cognitive impairment of a user, including the steps of:

(a) presenting a visual test stimulus to the user for a pre-determined exposure time;

(b) masking the test stimulus by placing a mask over or in place of the test stimulus;

(c) measuring a response from the user, the response including:

i. a response time; and

ii. a correct or incorrect indication of the visual test stimulus;

(d) repeating steps (a) to (c) to develop a user profile; and

(e) comparing the user profile to a standard profile to assess cognitive impairment in the user.

18. A system for assessing cognitive impairment of a user, including:

(a) means for presenting a visual test stimulus to the user for a pre-determined exposure time;

(b) mask for placement over or in place of the test stimulus after presentation of the visual stimulus;

(c) response measuring means to measure the response from the user after presentation of the visual test stimulus;

(d) processing means to process the response from the user over a range of pre-determined exposure times to develop the user profile over the range; and

(e) assessment means to compare the user profile to a standard profile to assess cognitive impairment in the user.

19. A mask for masking visual test stimulus, the mask including an image having a plurality of filled circles or parts thereof.

20. A method according to any one of claims 1 to 15 wherein the user profile is a response curve.

# ET Task — Presentation Sequence 1

**FIGURE 1A - Focal Point**

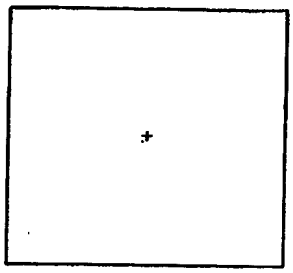


**FIGURE 1B - Test Stimuli**

OR

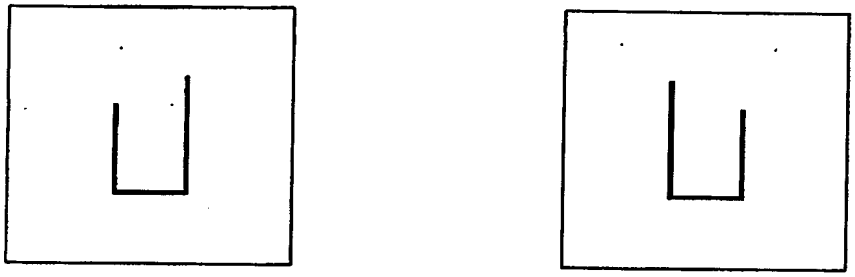
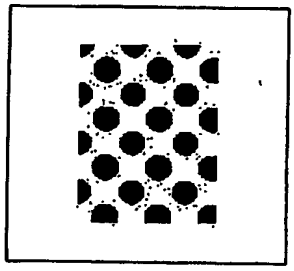


**FIGURE 1C - Backward Mask**



## ET Task — Presentation Sequence 2

**FIGURE 2A - Focal Point**

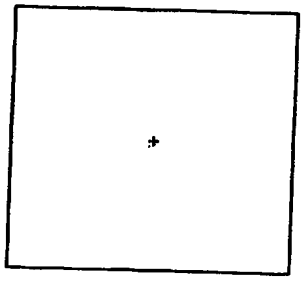
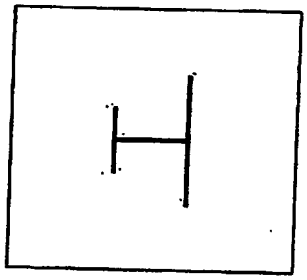


**FIGURE 2B - Test Stimuli**

OR



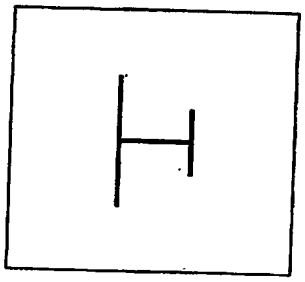
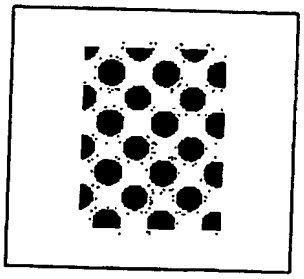


**FIGURE 2C - Backward Mask**



# ET Task — Presentation Sequence 3

**FIGURE 3A - Focal Point**

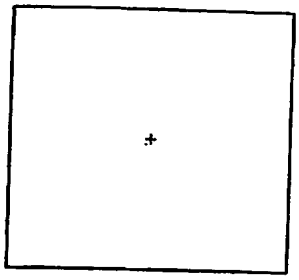
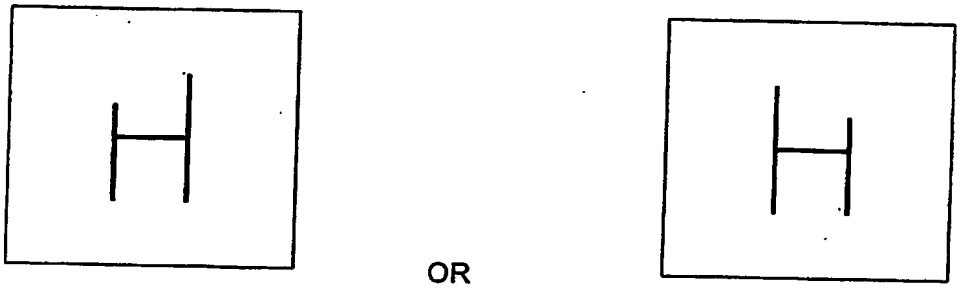
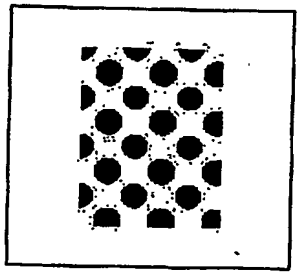


**FIGURE 3B - Test Stimuli**



OR

**FIGURE 3C - Backward Mask**



## ET Task — Presentation Sequence 4

**FIGURE 4A - Focal Point**

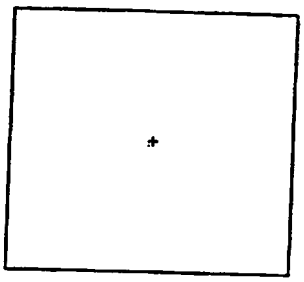


**FIGURE 4B - Test Stimuli**

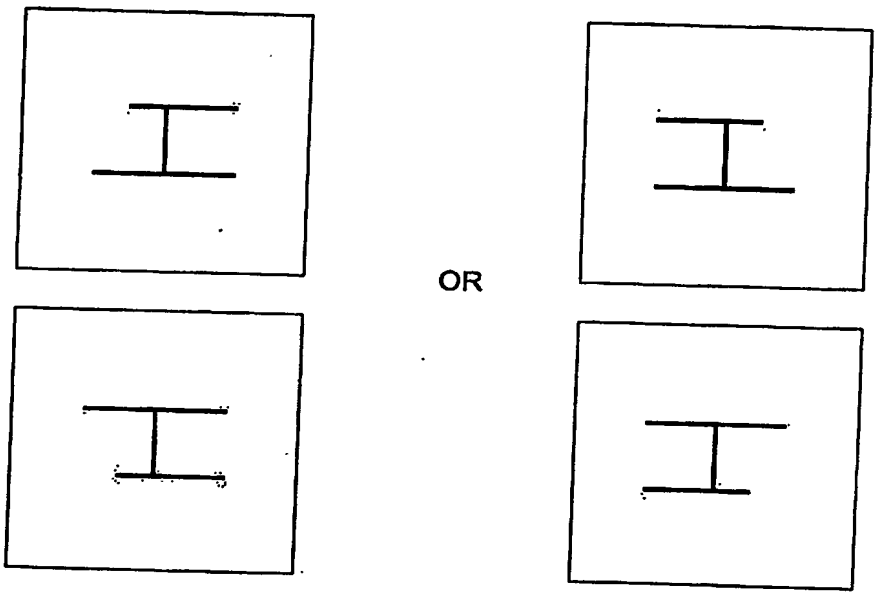
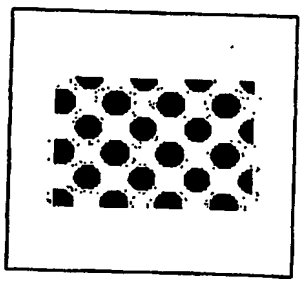
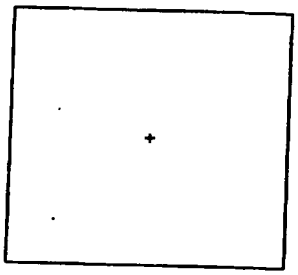



**FIGURE 4C - Backward Mask**



## VISUAL ACUITY Task (Vertical Stimuli) — Presentation Sequence

***FIGURE 5A*** **- Focal Point Stimulus**
Duration: 500 ms



***Test Stimulus***

**One of the 9 stimuli on the following page**

***FIGURE 5C*** **- Backward Mask**
Duration: 500 ms

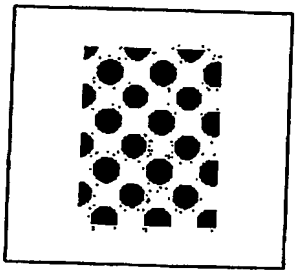
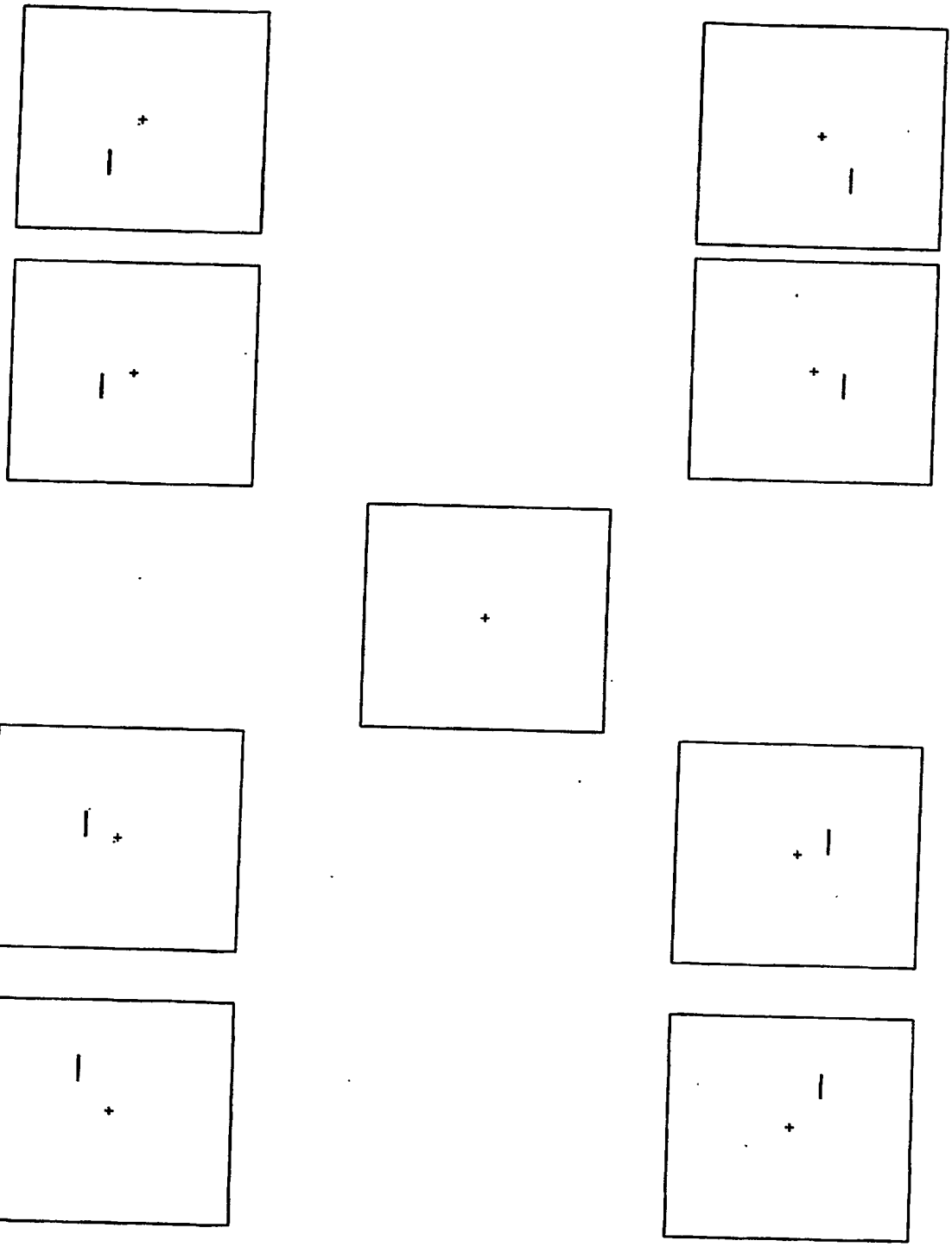
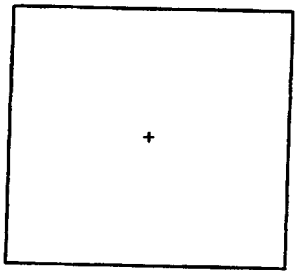


**FIGURE 5B - Target Stimuli**



## VISUAL ACUITY Task (Horizontal Stimuli) — Presentation Sequence

***FIGURE 6A*** **- Focal Point Stimulus**
Duration: 500 ms



***Test Stimulus***

**One of the 9 stimuli on the following page**

***FIGURE 6C*** **- Backward Mask**
Duration: 500 ms

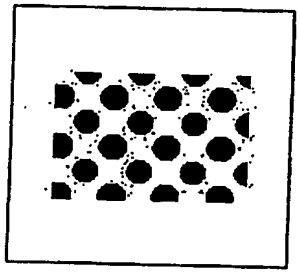


**FIGURE 6B - Target Stimuli**

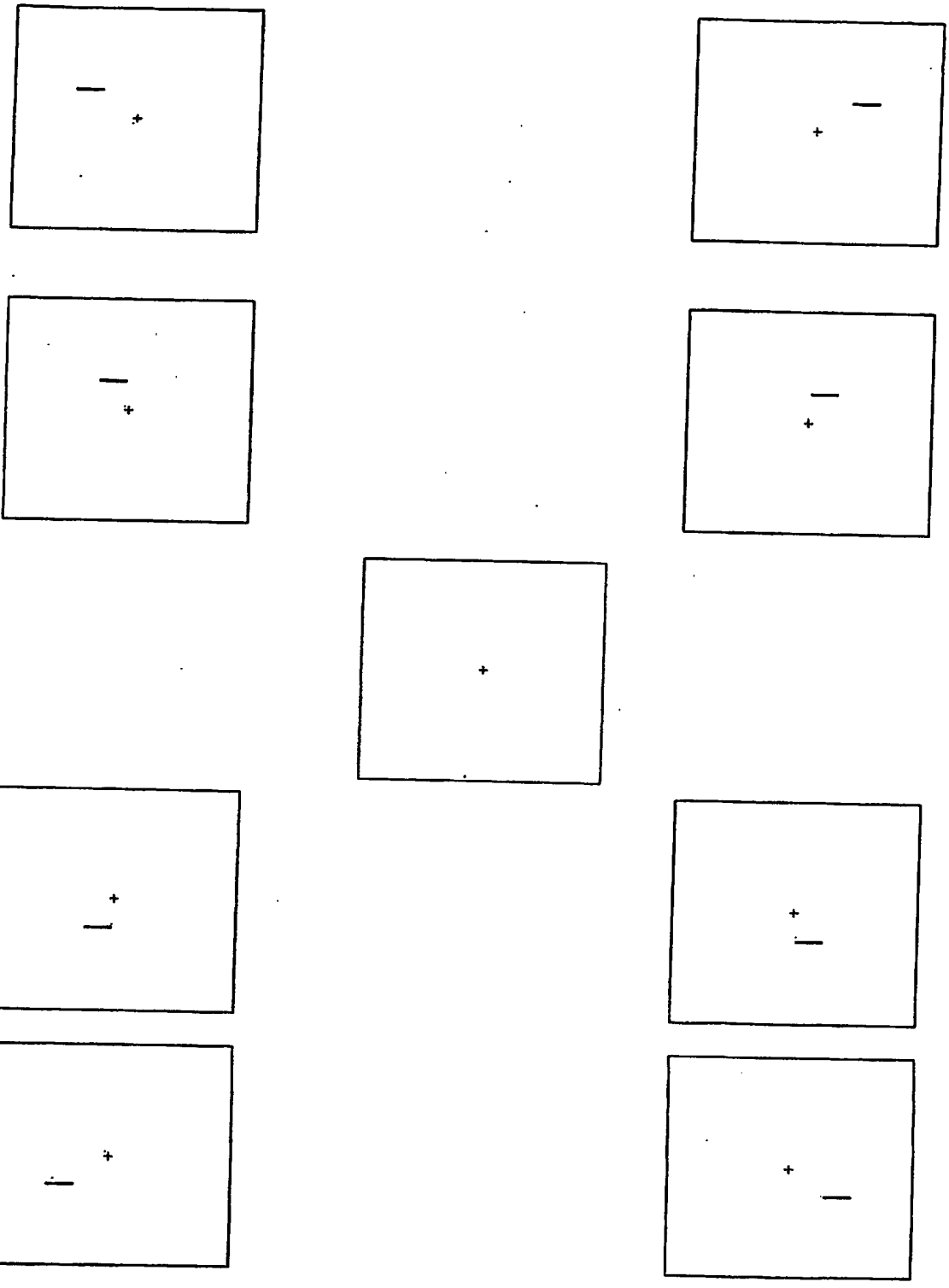


**FIGURE 7 - Error rate outcomes as a function of MMSE**

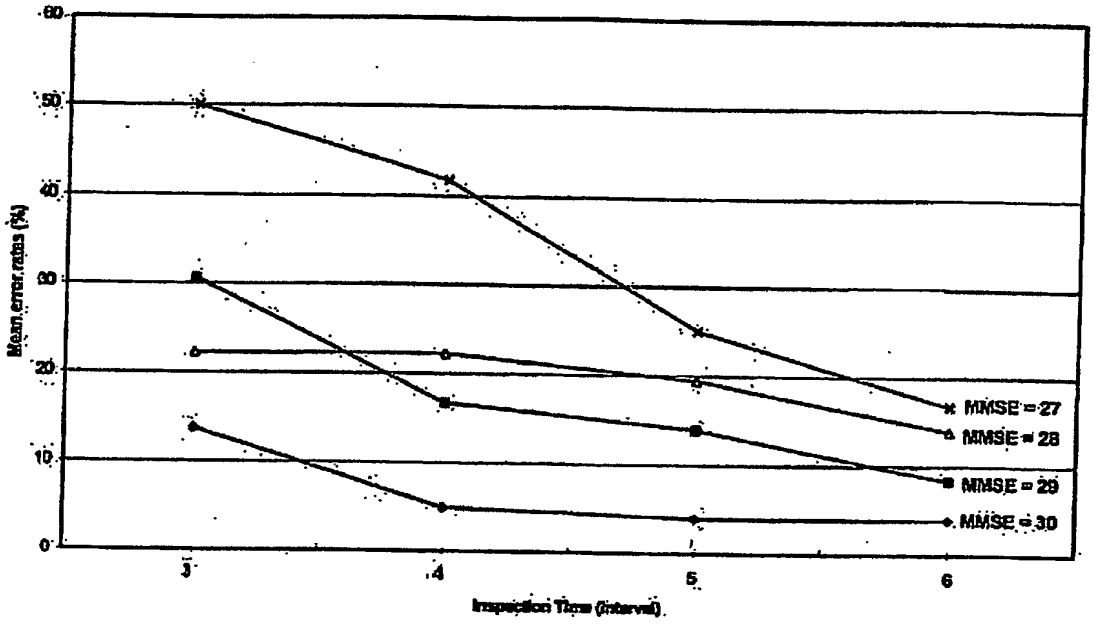


**FIGURE 8 - Response Time outcomes as a function of MMSE**